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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,179	02/01/2002	William A. Horne	480140.428C1	3580

500 7590 07/28/2005

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,179	HORNE ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/10/05 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant adds new claims 33-34, which are related to claims 30, 32 and are not new matter.

Accordingly, claims 30, 32-34 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION, NEW REJECTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 33-34 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 33-34 are drawn to a monoclonal antibody that specifically binds to an isolated human Bad polypeptide comprising the amino acid sequence of SEQ ID NO:2, or to a human Bad polypeptide consisting of the 95 contiguous amino acids of the carboxyl end of SEQ ID NO:2, wherein said monoclonal antibody interferes with the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide, or wherein said monoclonal antibody inhibits programmed cell death.

The specification discloses human Bad interacting polypeptides which can inhibit Bad activity by preventing the interaction of Bad with Bcl-2 or Bcl-X_L or other cell death regulatory molecules (p.11, lines 19-23). The specification also discloses that binding of human Bad to Bcl- X_L results in induction of programmed cell death (p.6, lines 21-23).

The specification however does not disclose the structure of specific epitopes of the claimed monoclonal antibodies, wherein said epitopes is necessary for the binding of Bad polypeptide to Bcl-2 or Bcl-X_L.

It is noted that Ottilie S et al, 1997, of record, teach that to date, domains in BAD necessary for binding to Bcl-2 or Bcl-X_L have not been identified (p.30866, second column, line 27-29, and that the BH3 domain (consisting of amino acids 103-124 of the claimed SEQ ID NO:2) is necessary for binding to Bcl-2 or Bcl-X_L (figure 4 on page 30869 in Ottilie S et al).

In other words, only after the filing of the claimed invention that the BH3 domain of human Bad, necessary for binding to Bcl-2 or Bcl-X_L is discovered.

It is further noted that not any monoclonal antibody of the genus of monoclonal antibodies binding to the whole amino acid sequence of SEQ ID NO:2 or to human Bad

polypeptide consisting of the 95 contiguous amino acids of the carboxyl end of SEQ ID NO:2 would interfere with the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide, or inhibit programmed cell death, because not any region of SEQ ID NO:2 or of the 95 contiguous amino acids of the carboxyl end of SEQ ID NO:2 is necessary for the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide.

The following teaching by the court, although drawn to a cDNA clearly applies to the claimed invention, *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials".Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to

> define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

In the instant application, the specification describes the claimed antibody by its function, without describing the structure of the specific epitope(s) of the claimed

antibody necessary for interfering with the binding of SEQ ID NO:2 to Bcl-2 or Bcl-X_L.

Thus the specification does not meet the written description requirement because "A definition by function, does not suffice to define the genus, because it is only an indication of what the gene does, rather than what it is", and because "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials".

Thus the specification fails to describe a monoclonal antibody that interferes with the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide, or that inhibits programmed cell death, by the test set out in the example of Lilly.

Further, the following teaching of the court as set out in Noelle also clearly applies to the instant claimed invention. The court teaches as follows: "Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen

at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application. Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen". *Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin* (CAFC, 02-1187, 1/20/2004).

In the instant application, the specification only discloses the full length polypeptide of SEQ ID NO:2, or the 95 contiguous amino acids of the carboxyl end of SEQ ID NO:2. The instant application does not however fully describe the specific epitope to which the claimed antibody binds. The specification fails to disclose the structural elements of the antigen of the claimed antibody that interferes with the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide, or that inhibits programmed cell death. The claimed antibodies are defined by their function of interfering with the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide, or inhibiting programmed cell death, not their physical structure.

Thus the specification fails to describe a monoclonal antibody that interferes with the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide, or that inhibits programmed cell death, by the test set out in the example of Noelle.

One of skill in the art would conclude that Applicant was not in possession of a monoclonal antibody that interferes with the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide, or that inhibits programmed cell death at the time of filing.

Thus, the specification does not provide an adequate written description of a monoclonal antibody that interferes with the binding of a human Bad polypeptide of SEQ ID NO:2 to a Bcl-2 or Bcl-X_L polypeptide, or that inhibits programmed cell death, that is required to practice the claimed invention.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a monoclonal antibody that specifically binds to a human Bad polypeptide "consisting of" the amino acid sequence of SEQ ID NO:2, does not reasonably provide enablement for a monoclonal antibody that specifically binds to a human Bad polypeptide "comprising" the amino acid sequence of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 30 is drawn to a monoclonal antibody that specifically binds to a human Bad polypeptide "comprising" the amino acid sequence of SEQ ID NO:2.

It is noted that due to the language "comprising" in claim 30, the encompassed claimed antibody could bind to the polypeptide comprising the polypeptide of SEQ ID NO:2, via an epitope from unrelated sequences that are adjacent the polypeptide of SEQ ID NO:2. In other words, the encompassed epitope of the claimed antibody is not known, and is not required to be within the polypeptide of SEQ ID NO:2.

Since the encompassed epitope of the claimed antibody cannot be determined, and is not required to be within the polypeptide of SEQ ID NO:2, one would not know how to make and use the claimed antibody.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

REJECTION UNDER 35 USC 102(e)

Rejection under 35 USC 102(e) of claims 30, 32 pertaining to anticipation by US 5,622,852 remains for reasons already of record in paper of 02/02/05.

Applicant argues that the Examiner has provided no basis for concluding that the antibody of '852 specific for a mouse Bad polypeptide would inherently bind to a human Bad polypeptide. Applicant argues that the human and mouse Bad polypeptides only share 75% homology, and this is not sufficient to conclude that the antibodies against one would necessarily cross-react with the other.

Applicant's arguments set forth in paper of 05/10/05 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that Kamarck et al, 1987, PNAS, USA, 1987, 84: 5350-5354, teach that there is extensive evidence for the existence of a family of 6-10 molecules that **share epitopes** (emphasis added) with CEA, and that because of these crossreactive antigens, CEA immunoassays do not necessarily detect only the CEA released by tumors (emphasis added) (p.5350, first column, last paragraph). Banki et al, 1994, JBC, 269 (4): 2847-51, teach that an antibody against human transaldolase could bind to yeast transaldolase which is about 58% homologous with human transaldolase, i.e. an antibody could cross-react and bind to a polypeptide at least with 58% homology to its antigen.

It is further noted that US 5,622,852 teaches production of monoclonal and polyclonal antibodies for mouse Bad polypeptide and fragments thereof (column 36, paragraph under Production and application of alpha-Bax antibodies).

US 5,622,852 further teaches that in some applications of these antibodies, where the object is, for example, to identify immunocrossreactive polypeptides that comprise a particular structural moiety, such as a bcl-2 binding domain, it is preferable that a fragment of Bad, such as BH1 or BH2 domain, rather than the entire native protein, is used as an antigen for making antiserum or monoclonal antibodies (column 37, lines 45-60).

The art monoclonal antibodies to mouse Bad polypeptide seem to be the same as the claimed monoclonal antibody, and would bind to human Bad polypeptide, in view

that there is no specific epitope of the monoclonal antibody that binds to SEQ ID NO:2 is recited in the claim 30, i.e. there is no particular monoclonal antibody that is bound to SEQ ID NO:2 recited in the claim, for the following reasons:

1) There would exist numerous shared epitopes of various monoclonal antibodies to the mouse Bad with the claimed monoclonal antibodies to the full length sequence SEQ ID NO:2 of 168 amino acids in length, in view of MPSRCH search report (of record), which shows 75% homology throughout the entire length of the sequence, and

2) An antibody could cross-react and bind to a polypeptide at least with 58% homology to its antigen, or to a polypepide sharing epitopes, as taught by Banki et al, supra, or Kamarck et al, supra.

Although the reference does not specifically teach that the monoclonal antibody would bind to SEQ ID NO:2, however, the claimed monoclonal antibody appears to be the same as the prior art monoclonal antibody. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Further, since the BH1 region of mouse BAD (amino acids 137-160) is within the corresponding 95 amino acids at the carboxyl end of SEQ ID NO:2 of the claimed

invention (amino acids 74-168 of SEQ ID NO:2) (see MPSRCH search report, of record), and since there is extensive homology between the BH1 region of the mouse Bad (amino acids 137-160) and corresponding region of the claimed SEQ ID NO:2, i.e. from a total of 24 amino acids of the BH1 region, there is only a difference of two amino acids, amino acids159-160, at the end of BH1 region, a monoclonal antibody to the BH1 region of mouse Bad would also bind to human Bad polypeptide consisting of 95 contiguous amino acids at the carboxy end of SEQ ID NO:2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

July 22, 2005